

## COLCHICUM: THE PANACEA

STANLEY L. WALLACE, M.D.

Associate Director of Medicine  
The Jewish Hospital and Medical Center of Brooklyn  
Brooklyn, N. Y.

THE history of colchicine is ancient and extensive. It has been reviewed recently in an excellent paper by Rodnan and Benedek.<sup>1</sup> In that paper, as in an earlier historical survey by Hartung,<sup>2</sup> the emphasis is, naturally enough, on the use of colchicum and other substances derived from the autumn crocus, *Colchicum autumnale*, in the treatment of acute gout.

But colchicum has been used in the treatment of many disorders other than gout. In 1763 Störck of Vienna was responsible for the modern reintroduction of extracts of the root of *C. autumnale* as therapy.<sup>3,4</sup> He described the drug as a diuretic, useful in dropsy, ascites, and anasarca. Störck first tested vinous extracts of the root on himself, and found them to increase the volume of his urine. The whole root, however, gave him abdominal pain, tenesmus, and diarrhea. On administration to a dog, whole root killed the animal after 13 hours of intense vomiting and diarrhea. Störck finally used a vinegar extract of the plant, sweetened by honey (an oxymel), and treated 13 dropsical patients with it. All had vigorous diuresis; several had failed to respond to extracts of squill.

In 1770 Husson introduced the Eau Médicinale as a panacea, effective in many diseases.<sup>5</sup> It was found to be especially useful in acute gout. In 1810 Jones reported remarkable effects of the Eau Médicinale d'Husson in gout.<sup>6</sup> The active ingredient in Eau Médicinale was shown by Want, in 1814, to be a vinous extract of the root of *C. autumnale*.<sup>7</sup>

Husson's extravagant claims for the Eau Médicinale are worthy of repetition.<sup>5</sup> He recommended it in the treatment of gout, sciatica, and rheumatism, and in madness (including postpartum psychosis), apoplexy, lethargy, catalepsy, paralysis, and epilepsy. He claimed that it strengthened the tired patient, the convalescent, those with weakness, nervous affections, and infirmities of old age. Eau Médicinale was also

recommended for obstipation, dysentery, worms (especially taenia), gastric and intestinal colic, indigestion, and poisoning with mercury and lead. It was useful also in scrofula, milk diseases, venereal diseases, smallpox, putrid inflammatory fevers, and cholera. It was of value in the treatment of rashes, scurvy, cancer, hydrops, asthma, and gravel. It relieved the pain of childbirth. It was recommended in the treatment of diseases of animals, including rabies. In fact, according to Husson, Eau Médicinale was useful in all seasons and climates, and was effective in all diseases except chronic ones, pulmonary disorders, fixed paralyses, polyyps, and internal tumors.

Once Want identified the active ingredient of the Eau Médicinale, colchicum gradually replaced it in the treatment of acute gout. From 1814 through the end of the 19th century, however, colchicum was used not only in acute gout, but in diseases imperfectly distinguished from gout (the rheumatisms); in diseases attributed to the gouty diathesis (e.g., neuritis and ophthalmia); and finally as a nonspecific anti-inflammatory agent in disorders known to bear no relation to gout, in the same manner as bleeding, leeching, cupping, and purging.

#### COLCHICUM AS AN ANTI-INFLAMMATORY AGENT

Haden, in 1820, published a monograph on the use of colchicum as a general remedy in the treatment of acute and chronic inflammatory diseases.<sup>8</sup> His father had begun to use colchicum in gout after Want's report. The father "then extended the use of the remedy from gout to rheumatism, and from the latter to the treatment of cases of inflammation in general."<sup>9</sup> Haden felt that colchicum was a substitute for bleeding in all disorders associated with increased action of the heart and arteries. He described its beneficial effects in rheumatic inflammatory fevers, inflammations of the lungs, catarrhs and influenza, and in puerperal fever. Others of his indications for its use included lumbago, pleurisy, bronchitis, mastitis, psoriasis, erysipelas ophthalmia, cutaneous ulcers, asthma, phthisis, quinsy, and hysteria and lowness of the spirits, among others.<sup>10</sup> In the period from October 10 through October 26, 1820, Haden treated 29 patients with colchicum. None had gout. The treatment was reported as curative or beneficial in all. In the same period he gave colchicum to his own three children, aged three and one half, two, and one, for colds with severe tracheal and laryngeal inflammation. All three children recovered.<sup>11</sup>

Armstrong<sup>12</sup> considered colchicum a medicine of considerable benefit in inflammatory fevers. He recommended it especially in acute or subacute rheumatism, and in internal serous inflammation, particularly of the arachnoid or of the pleura. For the treatment of dropsy, Armstrong recommended bleeding, purging, and a regulated diet, plus digitalis, squill, calomel, or colchicum.<sup>13</sup> He was the earliest to note that various preparations of colchicum lost their effectiveness on exposure to light.<sup>14</sup>

MacLagan reviewed the published experience with colchicum and described his own clinical studies.<sup>15</sup> He found colchicum useful as a diuretic in dropsy following scarlet fever, especially when the urine was suppressed and signs of coma were present. He recommended colchicum as an anti-inflammatory drug in acute gout, in acute articular rheumatism, and in urticaria.

Elliotson reported the beneficial effects of colchicum in erythema nodosum<sup>16</sup> and in pruritus.<sup>17</sup> Harvey successfully treated otitis media, mastoiditis,<sup>18</sup> scrofulous sore throat, and enlarged tonsils<sup>19</sup> with colchicum; he even recommended its external application to the neck for enlarged tonsils. Colchicum was said to be effective in the treatment of tetanus,<sup>20</sup> leukorrhea,<sup>21</sup> and in painful erections during gonorrhea and excessive sexual desire.<sup>22</sup>

#### COLCHICUM IN OTHER ARTICULAR DISEASES

Many individual reports described the beneficial effect of colchicum in the treatment of acute, subacute, and chronic rheumatism both in England and in the United States.<sup>23-30</sup> External application of the tincture of the root was also recommended for any kind of rheumatic pain.<sup>31</sup> In most of the reports the oral use of colchicum by mouth was accompanied by other modalities, most commonly bleeding and purging. Armstrong's suggestion<sup>30</sup> was typical: "If at an early period you abstract blood moderately from the arm so as to lessen the force and frequency of the heart's action and diminish the heat, purge the patient every morning, and give a drachm of vinum colchici at night: you will remove it [acute or subacute rheumatism] in a few days." In the treatment of chronic rheumatism, Armstrong recommended diet, purgation, liniments, exercise, hot baths, and colchicum.<sup>30</sup> Colchicum was also strongly advised in some of the complications of acute rheumatism: irregular pulse<sup>32</sup> and pericarditis.<sup>33</sup>

## COLCHICUM IN DISEASES THOUGHT TO BE RELATED TO GOUT

Benjamin Rush epitomized the concept of gout held by many physicians early in the 19th century, when he wrote: "The gout is a disease of the whole system. It affects the ligaments, blood vessels, stomach, bowels, brain, liver, lymphatics, nerves, muscles, cartilages, bones and skin."<sup>34</sup>

In the brain it [the gout] produces headache, vertigo, coma, apoplexy, and palsy. In the lungs, it produces pneumonia vera, notha, asthma, hemoptysis, pulmonary consumption and a short hacking cough. . . . In the throat it produces inflammatory angina. It affects the kidneys with inflammation, strangury, diabetes and calculi. . . . But of all the viscera, the liver suffers most from the gout. It produces in it inflammation, suppuration, melena, schirrus, gall-stones, jaundice, and an habitual increased secretion and excretion of bile.<sup>35</sup>

According to Rush, gout also caused loss of memory, madness, hysteria, hypochondriasis, and syncope. Angina pectoris, flatulence, vomiting, headache, piles and pruritis ani, urethral discharge and priapism; all were due to the gout.<sup>35</sup> Rush concluded: "The gout may be compared to a monarch whose empire is unlimited. The whole body crouches before it."<sup>36</sup> Rush's treatment of choice in gout, as in almost all other diseases, was heroic bleeding. But later was it not logical to use colchicum?

Graves<sup>37</sup> noted that gout caused trigeminal neuralgia, as well as grinding of the teeth, facial swelling, and bronchitis. Goss reported the successful treatment of trigeminal and median neuritides with colchicum.<sup>38</sup>

Later in the century, Hutchinson attributed repeated short attacks of conjunctivitis to gout.<sup>39</sup> In addition, destructive iritis and neuritis of the optic and third nerves, he felt, occurred chiefly in descendants of gouty individuals. A. Conan Doyle,<sup>40</sup> whose fame rests more on his literary than on his ophthalmologic labors, reported a family in which the grandfather had typical gout and died of chronic renal disease. His son had chronic eczema and psoriasis, and a granddaughter had intense pain in her eyes, accompanied by temporary congestion and partial blindness. Recognizing the granddaughter's symptoms to be gouty, and discovering the family history, Conan Doyle treated son and grand-

daughter with colchicum and alkalies. Needless to say, improvement in both was rapid.

### OTHER POINTS OF VIEW

In recent years there has been a dispute in regard to the diagnostic specificity of the response to colchicine. The evidence adduced above, however, hardly could serve as proof one way or the other. Such modern concepts as the use of one therapeutic agent at a time, a concern for objective as opposed to subjective responses, or the use of control groups were scarcely known.

Nevertheless, other points of view existed, suggesting that colchicum exerted its greatest effect in gout. Scudamore<sup>41</sup> recommended colchicum for acute gout, but not for acute or chronic rheumatism. Holland wrote that "the action of this medicine [colchicum] in rheumatic and other inflammations of the joints is certainly more ambiguous than in gout".<sup>42</sup>

It is particularly fitting to end this brief paper with Garrod, who stated that "we may sometimes diagnose gouty inflammation from any other form by noting the influence of colchicum upon its progress."<sup>43</sup> And "it is more important that we should not attempt to treat the disease [rheumatoid arthritis] in the same way as gout, for colchicum is for the most part injurious."<sup>44</sup> Finally, he reported that "Dr. Charcot, from his own observations, agrees with me that colchicum has but little power over rheumatic inflammation."<sup>45</sup>

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